APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,870	08/06/2001	Bernhard Palsson	066662-0092	1729

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EXAMINER
NEGIN, RUSSELL SCOTT

ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
05/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

SIP_Docket@mwe.com

	Application No.	Applicant(s)
	09/923,870	PALSSON, BERNHARD
Office Action Summary	Examiner	Art Unit	
	RUSSELL S. NEGIN	1631	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) OR THIRTY (30) DAYS,
WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed
  after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any
  earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on <u>01 February 2010</u>.

2a)☒ This action is **FINAL**.   2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is
closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) <u>49-52,56-60,64 and 68-83</u> is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) <u>49-52,56-60,64 and 68-83</u> is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All   b)☐ Some * c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage
        application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO/SB/08)
   Paper No(s)/Mail Date <u>2/1/2010</u>.

4)☐ Interview Summary (PTO-413)
   Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application
6)☐ Other: _____.

U.S. Patent and Trademark Office

PTOL-326 (Rev. 08-06)   **Office Action Summary**   Part of Paper No./Mail Date 20100428

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1 February 2010 has been entered.

Claims 49-52, 56-60, 64 and 68-83 are pending and examined in the instant Office action.

Information disclosure statements

The information disclosure statement filed on 1 February 2010 has been considered in part.

In order to advance prosecution, the IDS has been annotated to accurately reflect those pages or portions of websites which were submitted. In addition, the submitted portions of References 71, 74, 79, 81-82, 89-92, and 94 are cited in the correct form on the enclosed 892 form. Since the References are already in the file history, the references that are cited have NOT been enclosed with this Office action. To avoid duplication, References 71, 74, 79, 81-82, 89-92, and 94 are crossed out on the Information Disclosure Statement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set
> forth in section 102 of this title, if the differences between the subject matter sought to be patented and
> the prior art are such that the subject matter as a whole would have been obvious at the time the
> invention was made to a person having ordinary skill in the art to which said subject matter pertains.
> Patentability shall not be negatived by the manner in which the invention was made.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #1:

Claims 49-52, 56-60, and 68-83 are rejected under 35 U.S.C. 103(a) as being

unpatentable over Pramanik et al. [Biotechnology and Bioengineering, volume 56, 1997,

pages 398-421] in view of Blattner et al. [Science, volume 277, 1997, pages 1453-1469]

in view of Kunst et al. [Reviews in Microbiology, 1991, volume 142, pages 905-912].

Claim 49 is drawn to a method performed in a computer of simulating a metabolic

capability of an in silico strain of a microbe. The method comprises obtaining a plurality

of DNA sequences comprising most of the metabolic genes in a genome of the microbe,

to produce an in silico representation of a microbe. The method additionally comprises

determining open reading frames of genes of unknown function in the microbe in the

plurality of DNA sequences. The method additionally comprises assigning a potential

function to proteins encoded by the open reading frames by determining the homology

of the open reading frames to gene sequences encoding proteins of known function.

The method additionally comprises determining which of the open reading frames

potentially correspond to metabolic genes by determining if the assigned function of the

proteins is involved in cellular metabolism. The method additionally comprises

determining substrates, products, and stoichiometry of the reaction for each of the gene

products of the metabolic genes having an assigned function. The method additionally

comprises producing a genome specific stoichiometric matrix of the microbe produced

from said substrates, products and stoichiometry into a stoichiometric matrix. The

method additionally comprises determining a metabolic demand corresponding to a

biomass composition of the microbe. The method additionally comprises calculating

uptake rates of metabolites of the microbe. The method additionally comprises

combining the metabolic demands and the uptake rates with the stoichiometric matrix to

produce an in silico representation of the microbe. The method additionally comprises

incorporating a general linear programming problem to introduce an in silico strain of the

microbe. The method additionally comprises performing a flux balance analysis on the

in silico strain. The method additionally comprises providing a visual output to a user of

said analysis that simulated a metabolic capability of said strain predictive of the

microbe's phenotype.

          **In summary**, the method of claim 49 is drawn to assigning metabolic functions to

genes with unknown functions based on structural homologies to genes of known

functions in other organisms. This information is then used to predict and simulate the

metabolic capacity of an _in silico_ strain of a microbe.

          Claim 57 is drawn to a method performed in a computer for simulating a

metabolic capability of an in silico strain of a microbe analogous to the method of claim

49.

Claims 50 and 58 are further limiting wherein the microbe is question is E. coli.

Claims 51, 59, 68, 70-72, 75-76, 78-80, and 83 are further limiting wherein

cellular metabolism comprises central metabolism, carbohydrate assimilation, lipid and

fatty acid metabolism and nucleotide metabolism.

Claims 52 and 60 are further limiting wherein the assigning function comprises

performing BLAST.

The study of Pramanik et al. investigates the stoichiometric model of E. coli

metabolism, as stated in the abstract:

> A stoichiometric model of metabolism was developed to describe the balance of metabolic
> reactions during steady state growth of Escherichia coli on glucose (or metabolic intermediates)
> and mineral salts. The model incorporates 153 reversible and 147 irreversible reactions and 289
> metabolites from several metabolic data bases…

Consequently, Pramanik et al. studies many metabolic reactions that take place

within E. coli (i.e. see the list in Appendix A on pages 411-417). Equations 1 and 2 on

page 399 denote the flux model metabolism via a mass balance on E. coli wherein the

matrix S is a matrix of stoichiometric coefficients relevant to the equations.

Table VII on page 405 of Pramanik et al. lists the upper and lower bounds of

metabolite uptake and secretion, and the text under this table describes sensitivity of

each type of metabolism (i.e. aerobic or anaerobic) due to biomass composition. This

biomass and energy requirement (i.e. demand) is elaborated further under "Biomass

and energy requirements" in column 2 on page 399 of Pramanik et al.

Again, equations 1 and 2 on page 399 of Pramanik et al. represent a mass

balance on the metabolites of E. coli which combines the metabolic demands, uptake

rates and the stoichiometric matrix to produce an *in silico* representation of potential

functions of said microbe.

Page 403 of Pramanik et al., under "Sensitivity Analysis," lists a general linear

programming algorithm for solving equations 1 and 2 on page 399 of Pramanik et al.

Figure 3 on page 406 of Pramanik et al. illustrates a flux balance analysis on the

in silico strain of E. coli and provides visual output to a user that simulates a metabolic

capability of the strain.

However, Pramanik et al. does not teach obtaining a plurality of DNA sequences

comprising most of the metabolic genes in an genome, determining open reading

frames of these genes, assigning functions to the proteins encoded by the open reading

frames, and determining which of said open reading frames correspond to metabolic

genes. Additionally, Pramanik et al. does not teach determining open reading frames of

genes having an unknown function and assigning a function to their encoded products

based on homology to proteins in a different organism.

The study of Blattner et al. maps the complete genome sequence of Escherichia

coli K-12.

The final full paragraph of column 3 on page 1454 of Blattner et al. states, "The

genome of E. coli, diagrammed in Fig. 1, consists of 4,639,221 bp of complex DNA."

Consequently, Figure 1 on page 1465 of Blattner et al. illustrates an *in silico* map of the

complete genome of E. coli.

The first full paragraph of column 1 on page 1454 of Blattner et al. describes the

annotation process of identifying ORFs in genes constituting operons, regulatory sites,

mobile genetic elements, and repetitive sequences in the genome, assigning and

suggesting functions, and relating the E coli. sequence to other organisms. The second

full paragraph of column 1 on page 1454 states:

> Functions of previously known E. coli proteins were collected from the GenProtEC and EcoCyc
> database. The function of new translated sequences was inputted from sequence similarity.

Consequently, functions are assigned to proteins by determining similarities (i.e.

homologies) to proteins of known function.

The result of assigning functions to proteins is Table 4 on page 1459 of Blattner

et al. wherein metabolic genes are classified as such in their specific metabolic classes

listed in Table 4 of page 1459 of Blattner et al. One of the classes listed is nucleotide

synthesis and metabolism.

The first full paragraph of column 2 on page 1454 of Blattner et al. describes the

use of BLAST in assigning function to proteins.

Pramanik et al. and Blattner et al. do not teach determining open reading frames

of genes having an unknown function and assigning a function to their encoded

products based on homology to proteins in a different organism.

The review of Kunst et al. studies the project of sequencing the entire Bacillus

substilis genome. Applicant states in the paragraph bridging columns 1 and 2 on page

905 of Kunst et al.:

> At the first level of analysis, the DNA sequence will lead to a complete catalogue of putative
> protein sequences. These are likely to fall into one of 3 categories: (1) those whose functions
> are known, (2) those which show similarities with proteins identified in other organisms and which
> may have similar though not necessarily identical functions in *B. substilis*, and (3) those, probably
> the majority, whose function is unknown at present....

Consequently, the "unknown" functions of protein sequences are identifiable by homology comparison with corresponding sequences in other organisms. Such analysis allows the identification of function of two proteins with unknown function (see abstract of Kunst et al.).

Kunst et al. continue in the last paragraph of page 905:

> It will be of great interest to compare the sequence of the *B. substilis* genome with that of *E. coli*…. These organisms diverged about 1.2 billion years ago… It will be interesting to examine the conservation of "core" genes responsible for general metabolism.

Consequently, Kunst et al. express great interest in comparing the genomes of *E. coli* and *B. subtilis* as they pertain to metabolism.

Here is a chart illustrating where each of the species in claims 68-83 are found in the above prior art references:

Central metabolism	Claims 68, 76	Kuntz et al., introduction
Amino acid metabolism	Claims 69, 77	TCA cycle in Pramanik et al.
Nucleotide metabolism	Claims 70, 78	TCA cycle in Pramanik et al.
Fatty acid metabolism	Claims 71, 79	Pramanik et al., page 339, c2
Lipid metabolism	Claims 72, 80	Pramanik et al, page 339, c2
Vitamin/co factor synthesis	Claims 73, 81	Appendix A, Pramanik et al.
Energy and redox	Claims 74, 82	Appendix A, Pramanik et al.,
Carbohydrate assimilation	Claims 75, 83	Appendix A, Pramanik et al. and glycolysis

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the stoichiometric model of E. coli metabolism as taught by Pramanik et al. by use of the complete genome sequence of Blattner et al. wherein the motivation would have been that by knowledge of the full genome of E coli, not only can metabolism be further analyzed, but also knowledge of the entire sequence of E. coli enables global approaches to understanding biological function in living cells and has led to new ways of looking at the evolutionary history of bacteria [see first paragraph of introduction on page 1453]   It would have been further obvious to modify the stoichiometric model of E. coli metabolism as taught by Pramanik et al. and the complete E. coli genome structure in Blattner et al. by use of the comparison of E. coli and B. substilis metabolism genes and proteins to determine function of unknown proteins as in Kunst et al. wherein the motivation would have been that such homology comparisons allow for an analysis of the differences in evolution between the two different, but related, organisms to result in improvement in industrial applications [see last sentence on page 905 of Kunst et al. and first paragraph on page 906 of Kunst et al.].

Response to Arguments:

Applicant's arguments filed 1 February 2010 have been fully considered but they are not persuasive.

As a starting point, applicant bases most of the arguments on page 9-15 of the Remarks on two statistics in the reference of Blattner et al.:

> …more than one third of the open reading frames (ORFs) in the *E. coli* genome could not be
> attributed to a function and that close to two-thirds have no match in another organism… [Page 9
> of Remarks]

Throughout the Remarks, applicant relies on these statistics as bases to argue

against the expectation of success of combining Blattner et al. with Kunst et al. (i.e.

Blattner et al. and Kunst et al. are redundant and not complementary because both

studies lack sufficient knowledge of the respective genomes- pages 9 and 10 of

Remarks); motivation to combine Blattner et al. with Kunst et al. (i.e. since Blattner et al.

and Kunst et al. lack sufficient knowledge of the majority of genomes, no substantial

new information can be obtained on evolutionary history of a plurality of organisms-

page 12 of Remarks); and combining without use of hindsight reasoning (absent

sufficient knowledge of the majority of genomes, these documents can only be

combined in hindsight- page 12 of Remarks). It is noted that these arguments are

reiterated in applicant's summaries of the declarations of Keasling, Palsson, and

Nielsen on pages 13-15 of the Remarks.

These arguments are not persuasive for several reasons.

First, these statistics are taken out of context. The first statistic is listed in Table

4 of Blattner et al. lists 38.06% as the percentage of genes in *E. coli* with unknown

function. The second statistic, however, needs more investigating. Column 2 on page

1459 of Blattner et al. states:

> Nearly 60% of *E. coli* proteins have no match in any other COMPLETE genome considered.

However, the introductory paragraph on page 1453 of Blattner et al. reveals that

(at the time of publication of Blattner et al.) only six (6) COMPLETE genomes are

publicly available. Since only six genomes were considered, this 60% lack of homology

parameter does not seem to be a sufficient and representative number of genomes in

different organisms on which this calculation is to be based. Instead, this statistic is out

of context as it is only based on six other COMPLETE genomes and fully disregards

fragments of other genomes of other organisms that may have been known at the time

of this study.

        Second, even assuming (*en arguendo*) that these statistics are not taken out of

context, applicant uses relative and qualitative terms (i.e. "large," "most," "majority," and

"sizeable") to describe the unknown portions of genome structure and function. In view

of the specification and previous arguments, it is not known as to the quantitative

significance of each of these terms. Furthermore, the instantly rejected claims do not

recite a quantitative percentage of the genome structure and function that must be

known in order for the execution of the claim to be functional and successful.

Consequently, even if the above cited statistics are assumed to be accurate, there is no

evidence (or reason) as to why having knowledge of FUNCTION of "two-thirds" of the *E.*

coli genome and matching rate of HOMOLOGY of "40%" to the other six genomes is

insufficient and would result in an dysfunctional and non-combinable set of references

with a lack of reasonable expectation of success.

        To the contrary, as discussed above, the comparisons of the homologies

between two different, but related organisms results from the combination of Kunst et

al., Pramanik et al., and Blattner et al. Furthermore, there would have been a

reasonable expectation success in combining the stoichiometric matrices corresponding

to known biological functions in Pramanik et al. and Blattner et al. with the set of

sequences of Kunst et al., wherein a subset of the sequences has unknown biological

function, because the functions and structural stoichiometries of the relations in

Pramanik et al. are analogous to the kinetics of homologous organisms as taught in the

introduction of Kunst et al. Consequently, as there is this reasonable expectation of

success in combining Kunst et al. with Pramanik et al. and Blattner et al., and as Kunst

et al. takes analogous genomes and maps functions to genes of unknown function

based on structural homology with genes in other genomes with known function, Kunst

et al. adequately teaches the "missing piece" of Pramanik et al. and Blattner et al. This

teaching is characterized in the declaration summaries as what corresponds to what is

argued as the long-felt need. Consequently, as Kunst et al. directly teaches this nexus

(i.e. "missing piece"), these arguments in the declarations are also not persuasive

because this alleged "long-felt need" already is present in the prior art.

        In response to applicant's argument that the examiner's conclusion of

obviousness is based upon improper hindsight reasoning, it must be recognized that

any judgment on obviousness is in a sense necessarily a reconstruction based upon

hindsight reasoning. But so long as it takes into account only knowledge which was

within the level of ordinary skill at the time the claimed invention was made, and does

not include knowledge gleaned only from the applicant's disclosure, such a

reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA

1971).

The following rejection is reiterated:

35 U.S.C. 103 Rejection #2:

Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over

Pramanik et al. in view of Blattner et al. in view of Kunst et al. as applied to claims 49-52

and 56-60 above, and further in view of Xie et al. [TIBTECH, 1997, volume 15, pages

109-113].

Pramanik et al., Blattner et al., and Kunst et al. make obvious a method of

simulating a metabolic capability of an in silico strain of a microbe by simulating

metabolism within E. coli, as discussed above.

Pramanik et al., Blattner et al., and Kunst et al. do not teach calculation of uptake

rates by measuring depletion of substrate from the growth media.

The study of Xie et al. studies integrated approaches to the design of media and

feeding strategies for fed-batch cultures of animal cells.

Column 2 on page 109, lines 3-7 of Xie et al. states:

Obviously, a high viable cell density maintained for a long time is required to maximize product
concentration. However, this mainly depends upon the composition of the medium employed.

Consequently, the composition of the growth medium and its depletion over time

affects the growth of the cells.

The motivation of the study of Xie et al. is that by knowing this fact, better

compositions for culture media can be designed (i.e. see page 110 of Xie et al.)

It would have been obvious to someone of ordinary skill in the art at the time of

the instant invention to modify the metabolism studies of E. coli of Pramanik et al.

Blattner et al., and Kunst et al. by use of the nutrient depletion studies of Xie et al.

wherein the motivation would have been by knowing how nutrients are depleted in order

to facilitate cell growth, stronger media can be designed to enable better growth of the

cells in the cellular media [see page 110, column 1-2 under "Motivation for medium

design," and "Design of culture environment."] There would have been a reasonable

expectation of success in applying the animal cell study of Xie et al. to the bacterial

studies of Pramanik et al. and Blattner et al. because when all cells are cultured,

whether animal or bacterial, the cells need nutrients to survive, and as a result, all

species of cells deplete their culture media of these nutrients.

Response to Arguments:

Applicant's arguments filed 1 February 2010 have been fully considered but they

are not persuasive.

Applicant argues that the reference of Xie et al. does not overcome the alleged

deficiencies of the combination of references in the first 35 U.S.C. 103 rejection. This

argument is not persuasive because this combination of references teaches all of the

required limitations in the instantly rejected claims.

Double Patenting

The following rejection is reiterated from the previous Office action:

The nonstatutory double patenting rejection is based on a judicially created

doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees.   A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.2d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163

USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d)

may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of

activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a

terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with

37 CFR 3.73(b).

Claims 49-52, 56-60 and 64 are provisionally rejected on the ground of

nonstatutory obviousness-type double patenting as being unpatentable over claims 26-

28, 30, 32, 35-36, and 39-41 of copending Application No. 11/980,199. Although the

conflicting claims are not identical, they are not patentably distinct from each other

because the set of claims of the reference describes the same *in silico* process for open

reading frames, determining the metabolic capability of a strain of a microbe. For

instance, the steps of claim 30 of '199 correspond with the steps of instant independent

claim 49. Each claim has the steps of obtaining DNA sequences, determining ORFs,

assigning functions to proteins, determining which open reading frames correspond to

metabolic genes, determining a stoichiometric balance on relevant metabolic reactions,

determining metabolic demand, calculating uptake rates, combining metabolic demands

with uptake rates, incorporating general linear programming, performing a flux balance,

and providing visual outputs to a user.   Additionally claim 41 of the reference has steps

that correspond with the steps of instant independent claim 57.

This is a <u>provisional</u> obviousness-type double patenting rejection because the

conflicting claims have not in fact been patented.

Response to Arguments:

Applicant requests that this rejection be held in abeyance.

Conclusion

No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the

entry of the submission under 37 CFR 1.114 and could have been finally rejected on the

grounds and art of record in the next Office action if they had been entered in the

application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE**

FINAL even though it is a first action after the filing of a request for continued

examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE

MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later

than SIX MONTHS from the mailing date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by

facsimile transmission. Papers should be faxed to Technical Center 1600 via the

central PTO Fax Center. The faxing of such pages must conform with the notices

published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61

(November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)).

The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Russell Negin, whose telephone number is (571) 272-

1083. The examiner can normally be reached on Monday-Friday from 8:30 am to 5:30

pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571)

272-0720.

Information regarding the status of the application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information on the PAIR system, contact the Electronic Business Center

(EBC) at 866-217-9197 (toll-free).

/RSN/
Russell S. Negin

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631